IN THE UNITED STATES DISTRICT COURT
FOR THE EASTERN DISTRICT OF TEXAS
MARSHALL DIVISION

ERFINDERGEMEINSCHAFT UROPEP GbR,	§	
	§	
Plaintiff,	§	
	§	
v.	§	Case No. 2:15-CV-1202-WCB
	§	
ELI LILLY AND COMPANY, and BROOKSHIRE BROTHERS, INC.,	§	
	§	
Defendants.	§	

MEMORANDUM OPINION AND ORDER

In this patent case, the plaintiff, Erfindergemeinschaft UroPep GbR ("UroPep"), has alleged that the defendants, Eli Lilly and Company and Brookshire Brothers, Inc., have infringed U.S. Patent No. 8,791,124 ("the '124 patent"), owned by UroPep. Before the Court are two motions for summary judgment filed by the defendants: a motion for summary judgment of non-infringement, Dkt. No. 119, and a motion for partial summary judgment that claims 1 and 3 of the '124 patent are invalid for failure to meet the written description requirement of 35 U.S.C. § 112 ¶ 1, Dkt. No. 120.

Following a hearing on June 23, 2016, the Court entered an order construing several disputed terms of the '124 patent. Dkt. No. 131 (construing the terms "administering," "a person in need thereof," and "an effective amount"). In that order, the Court did not construe the term "an inhibitor of phosphodiesterase (PDE) V," which appears in the '124 patent, but instead postponed the construction of that term until summary judgment motions were filed. In addition, prior to issuing its claim construction order, the Court entered an amended docket control order setting forth a schedule for expedited briefing of the defendants' summary judgment motions.

Dkt. No. 117. In accordance with that schedule, the defendants filed motions for summary judgment of non-infringement and for partial summary judgment of invalidity. Those motions focus on the phrase "an inhibitor of phosphodiesterase (PDE) V."

In their non-infringement motion, the defendants argue that the disputed phrase should be construed under 35 U.S.C. § 112 ¶ 6 and that the scope of the claims should therefore be limited to certain specifically disclosed PDE V inhibitors. The necessary result of such an interpretation of the phrase, according to the defendants, would be a judgment of non-infringement. In their invalidity motion, the defendants argue that if the phrase "an inhibitor of phosphodiesterase (PDE) V" were construed to include all compounds capable of inhibiting PDE V (other than those specifically excluded by the claim language), the claims would lack the written description required under 35 U.S.C. § 112 ¶ 1, and therefore would be invalid.

UroPep responds that the phrase "an inhibitor of phosphodiesterase (PDE) V" should not be construed under 35 U.S.C. § 112 ¶ 6 and that construing the phrase without reference to 35 U.S.C. § 112 ¶ 6 does not give rise to a written description problem under 35 U.S.C. § 112 ¶ 1.

In this order, the Court construes the term "inhibitor of phosphodiesterase (PDE) V" and DENIES the defendants' two motions for summary judgment.

BACKGROUND

The '124 patent is directed to a method of treatment or prophylaxis of a person affected with benign prostatic hyperplasia ("BPH"), a condition associated with an enlarged prostate, leading to difficulty in urination and associated problems. By 1983, it was known that a significant improvement in the condition could be achieved by the administration of drugs that trigger the relaxation of the prostatic muscle cells. However, prior art treatments that relaxed those cells, such as the use of alpha-receptor blockers, were characterized by low effectiveness,

slow onset of action, or significant side effects. As an improvement over the prior art, the '124 patent purports to "have examined a completely different pharmacological principle of action, namely the affection of a key enzyme within the smooth muscle cells of the prostate gland, phosphodiesterase." '124 patent, col. 1, ll. 9-35.

The specification explains that the relaxation of smooth muscle cells is caused by the transmission of information through either hormones or neurotransmitters. That passage of information causes an increase in the levels of cyclic adenosine monophosphate ("cAMP") and cyclic guanosine monophosphate ("cGMP") in the muscle, which promotes the relaxation of those cells. The level of those compounds is reduced by the presence of phosphodiesterases ("PDEs"), which hydrolyze cAMP and cGMP. '124 patent, col. 1, ll. 36-52. To promote muscle relaxation, "[i]nhibitors of the PDEs in turn reduce the digestion of cAMP and cGMP, resulting in an increase of these molecules within the cell and thus in a relaxation of the smooth muscle cell." Id., col. 1, ll. 44-47. The '124 patent states that this mechanism of action had been described by a number of publications in the early 1990s. Id., col 1, ll. 48-52.

The '124 patent notes that the cited prior publications describe PDEs in the body as consisting of at least five categories of subesterases of PDE (i.e., PDE I to PDE V), and that the various PDEs are distributed differently throughout different organs and organ systems.[1] The specification asserts that the side effects and low effectiveness of the prior art prostate treatments suggests that "a well-aimed affection of the prostatic muscles by inhibiting a functionally important sPDE [specific PDE] isoenzyme appears to be superior to conventional therapy

[1] The specific PDEs were initially identified by Roman numerals, the convention followed in the '124 patent. It is now more common to use Arabic numerals to describe the specific PDEs. The current practice is to refer, for example, to PDE V as PDE5. For consistency, except where quoting record materials, the Court will use the Roman numeral convention that was commonly employed as of the July 1997 priority date of the'124 patent.

methods." '124 patent, col. 2, ll. 3-5. The specification states that PDE I, PDE IV, and PDE V have been found in prostate tissue and that a "well-aimed inhibition of these isoenzymes will result in relaxation of the [prostatic] muscles even when minute doses of a specific inhibitor are administered, with no appreciable effects in other organ strips." Id., col. 2, ll. 3-5. It then concludes that the "subject matter of the invention is the use of specific inhibitors of sPDE I, sPDE IV, and sPDE V in the prophylaxis and treatment of prostatic diseases, in particular [BPH] . . . ." Id., col. 2, ll. 17-20.

The '124 patent has one independent claim. It reads as follows:

> 1. A method for prophylaxis or treatment of benign prostatic hyperplasia comprising administering to a person in need thereof an effective amount of an inhibitor of phosphodiesterase (PDE) V excluding a compound selected from the group consisting of
>
> dipyridamole,
>
> 2-(N-(4-carboxypiperidine)-6-chloro-4(3,4-(methylendioxy)benzyl)amino)quinazoline,
>
> 2,3-dihydro-8-hydroxy-7-nitro-1,4-benzodioxine-2-methanol, alpha-nitrate.
>
> 4((3,4-(methylendioxy)benzyl)amino)-6,7,8-trimethoxy-quinazoline,
>
> 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one,
>
> 2-n-butyl-5-chloro-1-(2-chlorobenzyl)-4-methylacetate-imidazole,
>
> 1-cyclopentyl-3-methyl-6-(4-pyridinyl)pyrazolo(3,4-d)pyrimidin-4(5H)-one,
>
> 7-(3-(4-acetyl-3-hydroxy-2-propyl-phenoxy)-2-hydroxy-propoxy)-2-carboxy-2,3-didehydro-chronan-4-one,
>
> and pharmacologically compatible salts thereof.

’124 patent, col. 8, ll. 18-41 (emphasis added and duplicate compound removed).[2] In other words, the inventors “claimed a method of treatment for BPH by administering an effective amount of a PDE5 inhibitor” that is not one of the eight listed compounds or their pharmacologically compatible salts. Pl. UroPep’s Combined Sur-Reply to Defs.’ Mots. for Summ. J., at 11, Dkt. No. 141. Claim 3, which depends from claim 1, reads as follows:

> 3. The method of claim 1 wherein the compound in combination with a pharmacologically acceptable excipient is administered in a unit dose form.

’124 patent, col. 8, ll. 45-48.

The structure of claim 1, which covers all inhibitors of PDE V except for certain specifically listed compounds, is not common in the Court’s experience. As UroPep acknowledges “there are not a lot of claims that are drafted in this way.” Claim Construction Hr’g Tr., at 62:22-25, Dkt. No. 125.

The application for the ’124 patent was a continuation of the application that matured into U.S. Patent No. 8,106,061 (“the ’061 patent”). The ’061 patent includes claims that cover methods of treating of BPH and prostatic disease or relaxing prostatic muscles by administering a selective inhibitor of PDE IV and/or PDE V selected from a group of specific compounds. ’061 patent, col. 8, ll. 4-59. The specific compounds identified in the claims of the’061 patent include most of the compounds that are specifically excluded from the claims of the ’124 patent.

During the prosecution of the application that led to the ’124 patent, the examiner rejected the claims on the ground of nonstatutory double patenting. The patentees then amended claim 1 to exclude from the scope of the claim most of the PDE inhibitors recited in the ’061

[2] Claim 1, as set forth in the ’124 patent, contains a duplicate listing of 1-methyl-3-propyl-6-(5-(N-(4-methylmorpholino)sulfonyl)-2-ethoxyphenyl)pyrazole[4,5]pyrimidin-4(5H)one, which is one of the eight excluded compounds.

patent. Dkt. No. 106-08, at 115. When the examiner nonetheless rejected the new claims as being anticipated by the claims of the '061 patent, id. at 121-23, the patentees entered a terminal disclaimer with respect to the'061 patent, id. at 126-28. The claims were then allowed.

DISCUSSION

The matters presently before the Court raise three issues: (1) whether the term "an inhibitor of phosphodiesterase (PDE) V" in claim 1 of the '124 patent is governed by 35 U.S.C. § 112 ¶ 6; (2) how that term should be construed if it is not governed by section 112 paragraph 6; and (3) whether the specification of the '124 patent satisfies the written description requirement of 35 U.S.C. § 112 ¶ 1.

I. The Motion for Summary Judgment of Non-Infringement

UroPep's theory of infringement is that the defendants infringe, directly or indirectly, by the administration of the drug tadalafil (the active ingredient in Lilly's commercial product Cialis) to treat BPH. According to UroPep, tadalafil is "an inhibitor of phosphodiesterase (PDE) V" that is effective for prophylaxis or treatment of BPH, and its administration for that purpose therefore infringes UroPep's '124 patent.

The defendants' motion for summary judgment of non-infringement turns on the construction of the term "an inhibitor of phosphodiesterase (PDE) V." As noted, when the Court entered its claim construction order in this case, see Dkt. No. 131, it postponed construction of that term until briefing on the defendants' motions for summary judgment was complete. The Court will now construe that term.

UroPep proposes that the phrase "an inhibitor of phosphodiesterase (PDE) V" should be construed to mean a "compound able to inhibit phosphodiesterase (PDE) V." See Pl. UroPep's Corrected Opening Claim Constr. Br., at 21, Dkt. No. 105. In addition, UroPep asserts that the intrinsic record requires that the phrase should be understood to contain three additional

limitations: the PDE V inhibitor must be "selective"; it must consist of a small molecule; and it must be therapeutically effective.[3] See id. at 22-25; Pl. UroPep's Reply Claim Constr. Br., at 8-10, Dkt. No. 109.

The defendants argue that the term "an inhibitor of phosphodiesterase (PDE) V" is "an element in a claim for a combination" that recites function without reciting structure and therefore is governed by 35 U.S.C. § 112 ¶ 6. See Defs. Eli Lilly and Company and Brookshire Brothers, Inc.'s Resp. Claim Constr. Br., at 7-8, Dkt. No. 106. For that reason, they contend, only those compounds that are specifically described in the specification and not otherwise excluded would be covered by the claims. Construed in that manner, the patent would read only on zaprinast and MY5445, the only two non-excluded compounds that are specifically identified in the '124 specification as PDE V inhibitors and are not expressly excluded from the scope of the claims.

A. Analysis of the Term "an inhibitor of phosphodiesterase (PDE) V" Under 35 U.S.C. § 112 ¶ 6

The Court first addresses the question whether the term "an inhibitor of phosphodiesterase (PDE) V" is governed by 35 U.S.C. § 112, ¶ 6, the "means- (or step-) plus-function" clause of section 112 of the Patent Act.[4] Whether that clause applies to a particular claim element is a matter of claim construction and is therefore a question of law. Personalized Media Commc'ns, LLC v. Int'l Trade Comm'n, 161 F.3d 696, 702 (Fed. Cir. 1998).

[3] A selective inhibitor is one that inhibits a particular compound significantly more than it does others. For example, a selective inhibitor of PDE V would inhibit PDE V significantly more than it inhibits other PDEs, such as PDE II or PDE III. The parties dispute how selective a selective inhibitor must be in order to qualify as a "selective" inhibitor.

[4] Under the America Invents Act ("AIA"), section 112 paragraph 6 was recodified as 35 U.S.C. § 112(f). Although the AIA did not make any change in the substance of the provision, this opinion refers to it as section 112 paragraph 6, since the pre-AIA version of the provision governs cases involving the '124 patent.

Section 112 paragraph 6 was first enacted as part of the 1952 Patent Act "in response to Halliburton Oil Well Cementing Co. v. Walker, 329 U.S. 1 (1946), which rejected claims that do not describe the invention but use conveniently functional language at the exact point of novelty." Warner-Jenkinson Co. v. Hilton Davis Chem. Co., 520 U.S. 17, 27 (1997) (quoting Halliburton, 329 U.S. at 8); see also Gen. Elec. Co. v. Wabash Appliance Corp., 304 U.S. 364, 371 (1938). The statute allows functional claiming subject to certain restrictions. It provides as follows:

> An element in a claim for a combination may be expressed as a means or step for performing a specified function without the recital of structure, material, or acts in support thereof, and such claim shall be construed to cover the corresponding structure, material, or acts described in the specification and equivalents thereof.

35 U.S.C. § 112 ¶ 6 (2006).

1. Section 112 paragraph 6 as applied to method claims

The Federal Circuit has held that for method claims, such as the claims of the '124 patent, section 112 paragraph 6 "is implicated only when steps plus function without acts are present." Epcon Gas Sys., Inc. v. Bauer Compressors, Inc., 279 F.3d 1022, 1028 (Fed. Cir. 2002). As the Federal Circuit has explained, the word "means" in the statute refers to an apparatus element, which is implemented by structure or material, while the word "step" refers to a process element, which is implemented by an act. O.I. Corp. v. Tekmar Co., 115 F.3d 1576, 1582-83 (Fed. Cir. 1997). In other words, "structure and material go with means, acts go with steps." Id. at 1583. Overall, section 112 paragraph 6 is "implicated only when means *plus function* without definite structure are present, and that is similarly true with respect to steps, that the paragraph is implicated only when steps *plus function* without acts are present." Id. "The statute thus in effect provides that an element in a combination method or process claim may be recited as a

step for performing a specified function without the recital of acts in support of the function." Id.

Based on those Federal Circuit decisions, the Court concludes that means-plus-function analysis is not applicable to the method claims at issue in this case. The statutory provision permits a description of a claim "element" by function instead of structure, material, or act. 35 U.S.C. § 112, ¶ 6; see also Cole v. Kimberly-Clark Corp., 102 F.3d 524, 531 (Fed. Cir. 1996) ("[The Court] decide[s] on an element-by-element basis, based upon the patent and its prosecution history, whether § 112, ¶ 6 applies."); In re Fuetterer, 319 F.2d 259, 1460 n.11 (C.C.P.A. 1963) ("[Section 112, paragraph 6] in reality will give statutory sanction to combination claiming as it was understood before the Halliburton decision. All the [individual] *elements* of a combination now will be able to be claimed in terms of what they do as well as in terms of what they are.") (emphasis added) (quoting H.R. 3760, 82d Cong., 1st Sess., § 112 (1951) (statements of Representative Joseph R. Bryson, chairman of the subcommittee in charge of the legislation that resulted in the Patent Act of 1952)).

For method claims, the "elements" are acts; for apparatus claims, the "elements" are structures or materials. While a method element may describe the use of a structure or material, the "use" is still an act. Here, the reference to a PDE V inhibitor is not an element of the claims of the '124 patent; the element in question is the step of administering an effective amount of a PDE V inhibitor to a patient. Thus, even if means-plus-function analysis would apply to a product claim to "an inhibitor of PDE V," it does not apply to a method claim reciting a method of administering that substance to a patient. See O.I. Corp., 115 F.3d at 1583 ("[E]ven if we were to hold that the word 'passage' in the apparatus claims meets the section 112, ¶ 6, tests, we would not agree with [defendant] that the parallelism of the claims means that the method claims

should be subject to the requirements of section 112, ¶ 6"; instead, "[e]ach claim must be independently reviewed in order to determine if it is subject to the requirements of section 112, ¶ 6."); Epcon, 279 F.3d at 1028 (same).[5]

The inventive contribution of the patent is not the discovery or invention of PDE V inhibitors, which were both numerous and well-known at the time of the invention. Instead, the invention is based on the discovery that PDE V inhibitors can be effective in treating BPH. It is thus not the point of the patent to disclose or claim particular PDE V inhibitors; the point is to disclose and claim that PDE V inhibitors can be used to treat BPH. The patent is agnostic as to what PDE V inhibitor is used. It simply recites that by using an appropriate amount of a PDE V inhibitor, a therapeutic effect on BPH can be obtained.

In this respect, the reference in the '124 patent to a PDE V inhibitor is analogous to a reference, in a patent on a novel surgical procedure, to a cutting device that is used to begin the procedure. In such a patent, it is irrelevant what particular cutting device is used; that is not the point of the invention. In that setting, the reference to a cutting device would not implicate

[5] Notwithstanding the decisions in O.I. Corp. and Epcon, the Federal Circuit subsequently applied means-plus-function analysis to a method claim in On Demand Machine Corp. v. Ingram Industries, Inc., 442 F.3d 1331 (Fed. Cir. 2006). In that case, the claim limitation at issue recited "providing means for a customer to visually review said sales information." Id. at 1341. The Federal Circuit approved the district court's instruction to the jury that the "providing" limitation should be applied to the customer computer module disclosed in the specification plus its equivalents.

Although the defendants argue that the On Demand case shows that in appropriate cases means-plus-function analysis can be applied to method claims as well as apparatus claims, the Court disagrees. The parties in that case did not dispute that means-plus-function analysis was applicable, so the O.I. Corp. and Epcon decisions were never argued to the court. Moreover, the claims in the On Demand case expressly used the "means for" construction; the claims in that case could therefore be viewed as hybrid claims to which means-plus-function analysis might be applicable. No such "means for" language is present in the method claims of the '124 patent.

section 112 paragraph 6, and would not require that the patent be interpreted to read only on the particular cutting device or devices that may have been referred to in the specification.

Another similar example would be a patent that claimed a novel method for treating a particular type of cardiac arrhythmia by administering a blood thinner. Although the claim could be viewed as referring to the blood thinner by its function, the claim would not invoke section 112 paragraph 6, because the invention would be directed not to a new blood thinner, but to the use of the blood thinner (of whatever type) to treat a disease in a novel way. For that reason, the patentee would not be limited to any particular type of blood thinner that may have been referred to in the specification.

The same is true in this case. The point of the patent is not the invention of compounds that inhibit PDE V, but the invention of a treatment using compounds that have that effect. Thus, the '124 patent does not contain the flaw that led to the enactment of section 112 paragraph 6, by "us[ing] conveniently functional language at the exact point of novelty." Warner-Jenkinson, 520 U.S. at 27; Halliburton, 329 U.S. at 8; Gen. Elec., 304 U.S. at 371. For that reason, the use of the term "an inhibitor of phosphodiesterase (PDE) V" does not convert the claims of the '124 patent into the sort of claims to which section 112 paragraph 6 was meant to apply.

2. Section 112 paragraph 6 as applied to an "inhibitor of phosphodiesterase (PDE) V"

Even if means-plus-function analysis can apply to method claims in some instances, the Court concludes that the method claims at issue in this case are not in means-plus-function form.

The question whether section 112 paragraph 6 applies to a particular claim element turns on whether the words of the claim element would be understood by persons of ordinary skill in the art to have a sufficiently definite meaning as the name for a structure or an act. Williamson v. Citrix Online, LLC, 792 F.3d 1339, 1349 (Fed. Cir. 2015) (en banc). The use of the word

"means" in a claim element "creates a rebuttable presumption that § 112, para. 6 applies." Id. at 1347. On the other hand, "[w]hen a claim term lacks the word 'means,' the presumption can be overcome and § 112, para. 6 will apply if the challenger demonstrates that the claim term fails to 'recite sufficiently definite structure' or else recites 'function without reciting sufficient structure for performing that function.'" Id. at 1349. When section 112 paragraph 6 applies, it limits the functional term "to only the structure, materials, or acts described in the specification as corresponding to the claimed function and equivalents thereof." Id. at 1347.

Because the claims of the '124 patent do not contain the words "means for" (or "step for"), there is a rebuttable presumption that section 112 paragraph 6 does not apply to the term "an inhibitor of phosphodiesterase [PDE] V." For the reasons set forth below, the Court concludes that the defendants have not overcome that presumption by presenting evidence showing that a person of ordinary skill in the art as of the 1997 priority date of the '124 patent would have regarded "an inhibitor of phosphodiesterase [PDE] V" to be a purely functional limitation.

The defendants' position is that the term "an inhibitor of phosphodiesterase [PDE] V" describes the compound by what it does—i.e., it inhibits PDE V by any means—rather than by reference to a specific chemical structure. It is true that the term "inhibitor of phosphodiesterase (PDE) V" is described in part by its function. However, the fact that a thing is defined in part by its function does not necessarily compel the conclusion that a person of ordinary skill would not have a sufficiently definite idea of what that thing is. To the contrary, "[f]unctional language may [] be employed to limit the claims without using the means-plus-function format." Microprocessor Enhancement Corp. v. Tex. Instruments Inc., 520 F.3d 1367, 1375 (Fed. Cir. 2008); see also Lighting World, Inc. v. Birchwood Lighting, Inc., 382 F.3d 1354, 1360 (Fed. Cir.

2004) ("[T]he fact that a particular mechanism . . . is defined in functional terms is not sufficient to convert a claim element containing that term into a 'means for performing a specified function' within the meaning of section 112(6)."). That is because it is not uncommon for functional language to be used to describe particular structural objects, such as a brake, a drill, a lock, a putter, or a post-hole digger. In such cases, the name of the object is not congruent with the function suggested by the name: thus, for example, a driver is not a putter simply because a golfer decides to use his driver to putt, and a trowel is not a post-hole digger just because a gardener chooses to use the trowel to dig a post hole.

The "essential inquiry" in such cases is "whether the words of the claim are understood by persons of ordinary skill in the art to have a sufficiently definite meaning as the name for structure." Williamson, 792 F.3d at 1348; see also Greenberg v. Ethicon Endo-Surgery, Inc., 91 F.3d 1580, 1583 (Fed. Cir. 1996) ("What is important is not simply that [the term in question] is defined in terms of what it does, but that the term, as the name for structure, has a reasonably well understood meaning in the art."); Personalized Media Commc'ns, 161 F.3d at 704 (concluding that section 112 paragraph 6 did not apply to the term "detector" because, although defined in terms of its function, it "had a well-known meaning to those of skill in the art connotative of structure."). Moreover, it is not necessary that a term "connote a precise physical structure in order to avoid the ambit of [section 112 paragraph 6]." CCS Fitness, Inc. v. Brunswick Corp., 288 F.3d 1359, 1370 (Fed. Cir. 2002).

Based on the evidence of record, the Court finds that the defendants have failed to rebut the presumption that the term "inhibitor," which is used in the '124 patent without the word "means," does not invoke section 112 paragraph 6. In particular, the Court finds that the term

"an inhibitor of [PDE] V" is not merely the description of a function, but would convey structure to a person of skill in the art at the time of the invention.

The evidence before the Court shows that PDE V inhibitors have been "under investigation since around 1985" and "were well-understood by the time of the invention." Corrected Decl. of Nicholas K. Terrett, Ph.D., Regarding Claim Constr. of U.S. Patent No. 8,791,124 ("Terrett Decl."), at ¶ 21, Dkt. No. 105-1. By 1997, evidence of the general structure of the PDE V enzyme, as well as that of its cGMP-specific catalytic site, were reported in the literature. E.g., Michael Czarniecki et al., Inhibitors of Types I and V Phosphodiesterase: Elevation of cGMP as a Therapeutic Strategy, 31 ANN. REPORTS IN MED. CHEM. 61, 61-62 (1996) ("Czarniecki") (Phosphodiesterase "classes [including PDE V] share several common structural features and the amino acid sequences in the putative hydrolytic sites are highly conserved"; and the cDNA of PDE V, which "binds and selectively hydrolyzes cGMP," encodes "an 875 amino acid polypeptide with a homologous catalytic segment that is conserved across PDE types."), Dkt. No. 99-34; Kate Loughney & Ken Ferguson, 1. Identification and Quantification of PDE Isoenzymes and Subtypes by Molecular Biological Methods, in PHOSPHODIESTERASE INHIBITORS 1, 2 (Christian Schudt et al., eds., 1996) (PDEs, including PDE V, "share in common an arrangement of structural domains," including a "catalytic region [that] is localized in the carboxy-terminal portion of the protein."), Dkt. No. 99-35.

It is undisputed that, as understood in the art, "inhibitors" act by binding to the enzyme in a way that "inhibits," or suppresses, its catalytic activity. Nicholas Terrett, Ph.D., Dep., at 22:9-19 (May 26, 2016) (agreeing that "to inhibit an enzyme like PDE . . . a molecule binds to that enzyme and decreases its [catalytic] activity"), Dkt. No. 106-9; Decl. of David P. Rotella, Ph.D. in Support of Defs.' Mot. for Partial Summ. J. Regarding the Written Description of U.S. Patent

No. 8,791,124 ("Rotella Decl."), at ¶ 8(e) ("[an inhibitor of PDE V] encompasses compounds that may interact with the active site of the enzyme or some other site on the enzyme to inhibit activity"), Dkt. No. 121-4; see also Terrett Dep. at 15:25-16:22 (to inhibit the PDE V enzyme "means that the compound, the inhibitor, would [(a)] bind to the enzyme to make specific interactions with the catalytic site of the enzyme, and, thereby, prevent the phosphodiesterase from undertaking its normal catalytic activity," or (b) "bind to another site on the protein surface, a so-called allosteric site, … [to] block the [catalytic] activity of the enzyme."); David P. Rotella Dep. ("Rotella Dep."), at 71:12-72:16 (Aug. 24, 2016) (acknowledging PDE V inhibitors bind to the enzyme), Dkt. No. 130-1.

By the time of the invention, artisans had developed hundreds of PDE V inhibitors that bound competitively to the enzyme's catalytic site. Corrected Decl. of Dr. Andrew Bell in Support of Corrected Pl. UroPep's Combined Opp'n to Defs.' Mots. for Summ. J. ("Bell Decl."), at ¶¶ 45-47, 49 (noting that a review article published in 1995 contains evidence of more than 100 PDE V inhibitors, a 1995 patent now owned by Lilly lists 119 PDE V inhibitors, and a 1996 patent includes 55 examples of PDE V inhibitors), Dkt. No. 137-2. Indeed, it is undisputed even today that all known PDE V inhibitors bind competitively to the catalytic site of the enzyme. Bell Decl., at ¶ 50 (stating that, to his knowledge, "all PDE5 inhibitors bind to the same catalytic site on PDE5."); Terrett Dep., at 17:7-9 ("[A]ll of the PDE V inhibitors known do bind to the catalytic site."); Rotella Dep., at 71:12-16 (admitting that "all of the approved PDE5 inhibitors bind competitively with substrate [cGMP]."); see also Sharron R. Francis et al., Inhibition of Cyclic Nucleotide Phosphodiesterases by Methylxanthines and Related Compounds, 200 HANDBOOK OF EXP. PHARMACOL. 93, 94 (2011) ("Francis") ("All known PDE inhibitors contain

one or more rings that mimic the purine in the [cyclic nucleotide] substrate and directly compete with [the cyclic nucleotide] for access to the catalytic site."), Dkt. No. 99-37.

According to UroPep's expert, Dr. Andrew Bell, a review of the large numbers of PDE V inhibitors that were known in the art reveals "the overall structural similarity that [these] inhibitors have." Bell Decl., at ¶ 50. He concluded that all of the known PDE V inhibitors "share common physical structural features which include a planar region and typically a neighboring moiety capable of donating or accepting a hydrogen bond." Id. This result is unsurprising for two reasons. First, persons of skill in the art used known PDE inhibitors, such as zaprinast, "as the conceptual starting point for the design of new compounds." Terrett Decl., at ¶ 21 (quoting Czarniecki, at 62). For example, defendants' expert, Dr. David P. Rotella, used that approach in developing PDE V inhibitors. David P. Rotella et al., N-3-Substituted Imidazoquinazolinones: Potent and Selective PDE5 Inhibitors as Potential Agents for Treatment of Erectile Dysfunction, 43 J. MED. CHEM., no. 7, 2000, at 1257 ("[u]sing the prototypical PDE5 inhibitor zaprinast . . . as a template" to screen other potential PDE5 inhibitors), Dkt. No. 121-9; see also Rotella Dep., at 71:12-16 (noting use of a "template upon which inhibitors are based"). Second, persons of skill in the art at the time explored inhibitors that would mimic the structure of, and therefore compete with, cGMP to occupy the catalytic site of PDE V. E.g., Nicholas K. Terrett et al., Sildenafil (Viagra™), a Potent and Selective Inhibitor of Type 5 cGMP Phosphodiesterase with Utility for the Treatment of Male Erectile Dysfunction, 6 BIOORG. MED. CHEM. LETT., no. 15, 1996 at 1819, 1820-21 (in synthesizing potential PDE V inhibitors, relying on "[m]odelling studies [that] suggested that the nucleus may mimic the guanosine base of cGMP, as both are of similar size, shape and have a similar dipole moment," and considering that "extending the 3-substituent might fill a space in the enzyme active site occupied by ribose,

and substituents on the 5'-position of the phenyl ring could, depending on the conformation of cGMP in the enzyme active site, reproduce the role of the phosphate in binding"), Dkt. No. 121-12; see also Francis, at 94 (reporting that "[a]ll known PDE inhibitors contain one or more rings that mimic the purine in the [cyclic nucleotide] substrate and directly compete with [the cyclic nucleotide] for access to the catalytic site."), Dkt. No. 99-37.

This is not to say that "an inhibitor of PDE V" describes a fixed structure, or even a small subset of structures. Indeed, many authorities explain that PDE V inhibitors vary widely in structure. Terrett Decl., at ¶ 23; see also, e.g., Czarniecki, at 62 ("Significant structural latitude is possible while retaining potent inhibition of Type V PDE," and "there appears to be a wide tolerance for substitution [at certain positions of the inhibitor molecule]"), Dkt. No. 99-34. For that reason, Dr. Terrett stated that "[n]o one could know the range of compounds that could be included in that class." Terrett Dep., at 15:9-17. And, in response to counsel's question whether a person of skill in the art would "understand or know of a common chemical structure or feature for all inhibitors of PDE V," Dr. Terrett said no, as "[t]he PDE V inhibitors . . . represent a fairly diverse collection of different chemical structures." Id. at 25:17-22.

Yet even though PDE V inhibitors constitute a "diverse collection of different chemical structures," the evidence shows that they fall within the class of compounds designed to compete with cGMP to occupy the enzyme's catalytic site. Bell Decl., at ¶ 50. That class is not a small one, as Dr. Bell explained, because "the active site of the PDE5 enzyme accommodates such diversity." Id. at ¶ 51; see also id. at ¶¶ 51-55 (pointing out that the catalytic sites of some enzymes, such as COX and NMT, accommodate structurally diverse inhibitors, while those of other enzymes, such as CYP51, do not); Rotella Dep., at 78:1-14 (giving several examples of other enzyme inhibitors that show structural diversity similar to that of PDE V inhibitors). But

"[t]he fact that these [fundamental] physical structures can be accomplished through diverse chemical structures and that PDE5 inhibitors permit a variety of substituents does not take away from the overall structural similarity that inhibitors have, and must have, in order to bind to the catalytic site of the PDE5 enzyme." Bell Decl., at ¶ 50.

As such, "the words of the claim are understood by persons of ordinary skill in the art to have a sufficiently definite meaning as the name for structure." Williamson, 792 F.3d at 1349. Artisans understood that "an inhibitor" is a compound with a structure that can bind to a key site on the enzyme to inhibit its catalytic activity, and therefore developed inhibitors with structures complementary to particular portions of the enzyme's structure. In the case of PDE V, the artisans targeted the catalytic site and designed inhibitors with structures complementary to that site.

Put another way, the term "inhibitor of phosphodiesterase (PDE) V," as used in the '124 patent, is not simply a term that refers to any substance that will inhibit the chemical activity of PDE V. It does not apply, for example, to a very strong acidic solution which, when added to a solution containing PDE V, could be expected to destroy the PDE V molecules in a way that would disable their ability to hydrolyze cGMP. See also Terrett Decl., at ¶ 30 (noting that one of ordinary skill would not understand the patent to encompass techniques that "reduce the levels of PDE V enzyme in the cell" or that "insert a mutation into the gene(s) encoding the PDE V enzyme" to "disrupt its structure," as that would be inconsistent with the understanding of the term "inhibitor"). Instead, as both parties' experts attest, "an inhibitor" refers to a category of compounds with certain physical structures that bind to PDE V molecules in a way that prevents them from hydrolyzing cGMP.

In construing claims in light of section 112 paragraph 6, it is important to confine that statutory provision to cases for which it was designed to apply, and not to apply it mechanically whenever any seemingly functional term appears anywhere in a claim. That provision allows drafters to describe a structure, material, or act by its function, with the understanding that the structure, material, or act will be limited by what is disclosed in the specification. Drafters should not, however, be confined by section 112 paragraph 6 when they use a term that is understood by persons of skill in the art to have a meaning that denotes structure, even though the term may also describe the function performed by the object in question. Instead, in such cases the conventional tools of claim construction should be applied to discern the scope of the term. See Hill-Rom Servs., Inc. v. Stryker Corp., 755 F.3d 1367, 1374-75 (Fed. Cir. 2014); Greenberg, 91 F.3d at 1583.

For example, in Personalized Media Communications, LLC v. International Trade Commission, which involved a patent claiming a receiver system that detects and manipulates digital control signals in a broadcast or cablecast transmission, the Federal Circuit rejected the Commission's argument that "detector" should be read as a means-plus-function limitation. 161 F.3d 696, 704 (Fed. Cir. 1998). The term was "not a generic structural term such as 'means,' 'element,' or 'device,'" and it "had a well-known meaning to those of skill in the electrical arts connotative of structure." Id. The court acknowledged "the fact that a 'detector' is defined in terms of its function" and "does not connote a precise physical structure in the minds of those of skill in the art." Id. at 705. But, "[e]ven though the term 'detector' does not specifically evoke a particular structure, it does convey to one knowledgeable in the art a variety of structures known as 'detectors.'" Id. Therefore, the term "detector" was "a sufficiently definite structural term to preclude the application of § 112, ¶ 6." Id.

Like the term "detector" in Personalized Media Communications, the term "inhibitor" in this case presents a good example of an instance in which a seemingly functional term does not play the role in the claim that section 112 paragraph 6 was directed to and therefore does not trigger the application of that provision. See also, e.g., CCS Fitness, 288 F.3d at 1369 (concluding that section 112 paragraph 6 did not apply to "reciprocating member" because a person of ordinary skill in the art would understand the term to connote beam-like structures encompassing more than the "single-component, straight bar structures (and their equivalents) shown in the patents' drawings.").

The observations of the defendants' expert, Dr. Rotella, are not inconsistent with this conclusion. Dr. Rotella agreed that all known PDE V inhibitors bind to the enzyme's cGMP catalytic site. Rotella Dep., at 71:12-16;[6] see also Rotella Decl., at ¶¶ 101, 103 (describing the method of determining how an inhibitor binds to PDE V by combining the inhibitor with a fragment of the PDE V molecule that includes the cGMP catalytic site, rather than the whole enzyme), Dkt. No. 121-3. He then explained that inhibitors may vary in structure and have different binding interactions with PDE V. Rotella Decl., at ¶ 33; see also, e.g., Rotella Decl., at ¶ 102 (comparing how structural features of tadalafil and sildenafil bind to various pockets within the catalytic site of PDE V). Dr. Rotella focused on minute differences in binding interactions and made the general statement that "there is no structure that would be common to all compounds able to inhibit PDE5." Rotella Decl., at ¶ 19. But he never described any particular PDE V inhibitor as lacking the fundamental structures identified by Dr. Bell that

[6] Dr. Rotella mentioned "one paper" that he "believe[d]" was "published in 2005 that illustrates that it is possible to inhibit PDE V by binding at a site distinct from the active site." Rotella Dep., at 71:18-22. But he could not remember the name of the lead author on the paper, id. at 72:6-16, and the defendants have submitted nothing to supplement that statement. Dr. Bell stated that he was not aware of any such paper or similar evidence. Bell Decl., at ¶ 50.

account for "the overall structural similarity that [PDE V] inhibitors have, and must have, in order to bind to the catalytic site of the PDE5 enzyme." Bell Decl., at ¶ 50. More importantly, Dr. Rotella's review of how certain inhibitor molecules may differ—for example, by including other components that bind to additional regions of the catalytic site—does not undermine the experts' agreement that all PDE V inhibitors bind to the enzyme and therefore have structures that correspond to that of PDE V.

The evidence, of course, does not show—nor does UroPep attempt to argue—that simply stating that a compound is a PDE V inhibitor would resolve all the questions that might have come to the mind of a person of ordinary skill about its nature. Clearly there are issues as to additional properties of the compound that a person of ordinary skill would consider, such as its precise chemical composition, its toxicity, its selectivity, and its kinetics. Thus, a person of skill in the art would need to have additional information in order to describe a particular PDE V inhibitor in detail, just as a golfer would need additional information beyond the term "putter" to describe a particular type of putter in detail. However, the Court finds that those additional questions do not rise to a level such that a person of ordinary skill would lack a reasonably definite understanding of the structure in question.

In sum, a person of ordinary skill in the art as of the priority date of the '124 patent would have had a reasonably certain understanding of the structural features necessary for a particular compound to be an inhibitor of PDE V, as that term was used in the field. For that reason, the Court finds that the defendants have not carried their burden to overcome the presumption that 35 U.S.C. § 112 ¶ 6 does not apply to the term "an inhibitor of phosphodiesterase (PDE) V."

B. Construction of the Term "an inhibitor of phosphodiesterase (PDE) V"

The parties agree that if section 112 paragraph 6 does not apply to the term "an inhibitor of phosphodiesterase (PDE) V," the term should be construed to mean "a compound able to inhibit PDE V." However, UroPep argues that the term should be given an even narrower construction in three respects: first, the compound must be a "small molecule" compound; second, it must be "therapeutically effective"; and third, it must be "relatively selective" as to PDE V. The defendants disagree and argue that the term is not limited in any of those three additional respects.

1. Small molecule compound

The Court agrees with the parties that "an inhibitor of phosphodiesterase (PDE) V" refers to a compound, as is clear from the claim language. The phrase "an inhibitor of phosphodiesterase (PDE) V" is followed by the limitation that it "exclud[es] a compound selected from the group" of eight listed compounds. That formulation, although unusual, is a modified form of a claim to a Markush group, which is "a listing of specified alternatives of a group in a patent claim, typically expressed as "a member selected from the group consisting of A, B, and C." Abbott Labs. v. Baxter Pharm. Prods., Inc., 334 F.3d 1274, 1280 (Fed. Cir. 2003). Because the term "an inhibitor of phosphodiesterase (PDE) V" is defined, albeit in negative form, by reference to a group of compounds, the claim language suggests that "an inhibitor of phosphodiesterase (PDE) V" must be a compound, like the compounds that are excluded from its coverage. Moreover, as the defendants have noted, "the specification of the '124 Patent . . . uses the terms 'inhibitor,' 'compound' and 'substance' interchangeably." Defs. Eli Lilly and Company and Brookshire Brothers, Inc.'s Resp. Claim Constr. Br., at 8, Dkt. No. 106.

The dispute between the parties centers on whether the term "inhibitor" is limited to a compound of a particular size. UroPep argues that "inhibitor," as used in the '124 patent, is limited to a "small molecule compound." UroPep adopts that position based on the testimony of its expert, Dr. Terrett, who stated in his declaration that the "inhibitor of phosphodiesterase (PDE) V" referred to in the '124 patent must be a compound whose molecular weight does not exceed about 600 Daltons. He stated:

> Small molecule compounds are formed by the combination of multiple atoms in a specifically defined structural arrangement. Such compounds are referred to as small molecules if the total molecular weight does not exceed around 600 Daltons. The definition also distinguishes the compounds from larger molecules such as peptides, proteins or polymers. An individual compound has a unique chemical structure that confers the compound's pharmacological and physical properties, and no alteration of the connections between atoms is permitted as such change would redefine the identity of the compound.

Terrett Decl., at ¶ 22. While Dr. Terrett's definition of "small molecule compounds" may be consistent with the definition of a small molecule compound in the art, nothing in the record suggests that the term "inhibitor," as used in the '124 patent, is limited to a compound having a molecular weight under a particular limit, such as 600 Daltons. The Court therefore does not adopt UroPep's contention that the term "an inhibitor of phosphodiesterase (PDE) V" is limited to "small molecule" compounds, as defined by Dr. Terrett.

2. Therapeutically effective

UroPep next argues that the term "an inhibitor of phosphodiesterase (PDE) V" requires that the inhibitor be therapeutically effective. The Court disagrees. The "inhibitor of phosphodiesterase (PDE) V" is simply a compound that inhibits PDE V. Of course, claim 1 of the '124 patent describes a "method of prophylaxis or treatment of [BPH] comprising administering . . . an effective amount of an inhibitor of phosphodiesterase (PDE) V." Therefore,

the claim separately requires that the administration of the PDE V inhibitor be "effective" in the "prophylaxis or treatment of [BPH]." For that reason, a particular inhibitor of PDE V may be insufficiently potent to be effective in treating BPH, in which case a treatment using that inhibitor would not satisfy the "effective amount" limitation of the claims. But nothing in the record supports UroPep's contention that the requirement of effectiveness in treating BPH is inherent in the definition of the term "inhibitor of phosphodiesterase (PDE) V."

3. Selective inhibitor

Finally, UroPep argues that the claimed inhibitor of PDE V must be a selective inhibitor, i.e., a compound that inhibits PDE V to a significantly greater extent than other specific PDEs. UroPep's position is that "statements made during the prosecution of the '124 patent family confirm that the claims cover the use of selective inhibitors." Pl. UroPep's Corrected Opening Claim Constr. Br., at 23 (citing portions of the prosecution history of the parent application and stating that "patentees thus distinguished its invention over the prior art by emphasizing the selective nature of the PDE V inhibitors"), Dkt. No. 105; see also Pl. UroPep's Reply Claim Constr. Br., at 2 n.2 (citing statements made during the prosecution of the parent application), Dkt. No. 109.

The defendants respond to UroPep's argument by pointing out that the patentees claimed "a selective inhibitor" in the patent that issued from the parent application and therefore knew how to claim that the inhibitors in the '124 patent were "selective" if that is what was intended. The failure to include the term "selective" in the claims of the '124 patent, according to the defendants, is a clear indication that the reference to "an inhibitor of phosphodiesterase (PDE) V" in that patent was not intended to be limited to "selective" inhibitors of PDE V, as was the

case for the earlier patent. Defs. Eli Lilly and Company and Brookshire Brothers, Inc.'s Resp. Claim Constr. Br., at 15-16, Dkt. No. 106.

The Court finds that the term "inhibitor of phosphodiesterase (PDE) V" in the '124 patent refers to a selective inhibitor of PDE V. The specification of the '124 patent makes clear that a PDE V inhibitor is a member of the class of specific PDE inhibitors, or sPDEs. '124 patent, col. 1, line 53, through col. 2, line 16; col. 7, line 35, through col. 8, line 27. The specification further explains that a substance is considered an inhibitor of a specific PDE if the amount of that substance needed to hydrolyze the specific PDE is much less than the amount needed to hydrolyze other specific PDEs. Id., col. 8, ll. 5-9.

In addition, the prosecution history supports the conclusion that the term "inhibitor of phosphodiesterase (PDE) V" refers to a selective PDE inhibitor. The application for the '124 patent was a continuation of application number 10/443,870, which matured into the '061 patent. As noted, the '061 patent claimed many of the compounds that were expressly excluded from the claims of the '124 patent. In the prosecution of that application, the applicants distinguished the claimed compounds from the compounds disclosed in a prior art reference on the ground that the prior art reference did not teach the use of a specific PDE V inhibitor for treating prostate hypertrophy, see Oct. 27, 2009, Am. and Remarks, at 10, Dkt. No. 99-26. The applicants asserted that "[t]he compounds of the currently pending claims are selective inhibitors," unlike the compounds disclosed in the prior art, see Mar. 7, 2010, Am. and Remarks, at 10, Dkt. No. 99-27. Thus, in the course of the prosecution of the '061 patent, the applicants clearly disclaimed non-selective inhibitors (and amended the claims in accordance with that disclaimer). The question is whether the disclaimer that the applicants made during the prosecution of the '061 patent applies to the continuation application that led to the '124 patent.

In general, a prosecution disclaimer "will only apply to a subsequent patent if that patent contains the same claim limitation as its predecessor." Regents of Univ. of Minn. v. AGA Med. Corp., 717 F.3d 929, 943 (Fed. Cir. 2013). Where the limitations are different, the question whether the disclaimer is to be carried forward turns on whether there is a material difference between the earlier and later claim limitations. Id. at 944. However, there is "an exception [to that rule] where an amendment to a related limitation in the parent application distinguishes prior art and thereby specifically disclaims a later (though differently worded) limitation in the continuation application." Invitrogen Corp. v. Clontech Labs., Inc., 429 F.3d 1052, 1078 (Fed. Cir. 2005) (citing Elkay Mfg. Co. v. EBCO Mfg. Co., 192 F.3d 973, 978-79 (Fed. Cir. 1999)). Here, the patentees amended their claims during the prosecution of the parent '061 patent to overcome a prior art rejection by arguing that its inhibitors of PDE IV and/or PDE V were "selective." Therefore, it does not matter that UroPep did not affirmatively include that limitation in the '124 patent; the limitation was included through the earlier disclaimer and amendment. Even if that were not true, it would be difficult to imagine one of ordinary skill reading the specification of the '124 patent and concluding that the reference to an inhibitor of PDE V was not meant to be limited to a selective inhibitor. See, e.g., '124 patent, col. 2, ll. 3-4 ("a well-aimed affection of the prostatic muscles by inhibiting a functionally important sPDE isoenzyme"); col. 2, line 28 ("[p]referred selective inhibitors of PDE I, IV, and V").[7]

[7] The defendants assert that Housey Pharms., Inc. v. Astrazeneca UK Ltd., 366 F.3d 1348 (Fed. Cir. 2004), stands for the proposition that the inhibitor claimed in the '124 patent cannot be selective because the claim language does not include the terms "selective" or "relatively selective." Housey does not stand for such a broad proposition. In determining the correct construction of the term at issue in that case, the Housey court considered both the prosecution history and the specification, and it concluded that they did not support the argument that the claim term in question should be given a restrictive construction. Id. at 1354-55. Having considered both the prosecution history and the specification in this case, the Court concludes

The parties also dispute how great the differential effect must be for a compound to be considered a "selective" inhibitor. On this issue, the specification of the'124 patent provides helpful guidance. The specification states that an inhibitor is a considered an inhibitor of a specific PDE "if the concentration thereof which is necessary for inhibiting 50% of the substrate hydrolysis (IC_{50}) is at least 20 times lower in the respective peak fraction containing the specific phosphodiesterase than in other peak fractions." '124 patent, col. 8, ll. 6-9. The parties do not appear to dispute that this "20 times" standard represents the general understanding of a person of ordinary skill in the art. The Court therefore finds that a selective inhibitor of a specific PDE is at least 20 times more effective in inhibiting that specific PDE as compared to all other specific PDEs.

In summary, the Court finds that "an inhibitor of phosphodiesterase (PDE) V" is "a compound that selectively inhibits PDE V."

C. The Motion for Summary Judgment of Non-Infringement Is Denied

As noted earlier, the defendants' motion for summary judgment of non-infringement was predicated on their assertion that the claims of the '124 patent are governed by 35 U.S.C. § 112 ¶ 6. In the course of construing the term "inhibitor of phosphodiesterase (PDE) V," the Court has found otherwise. The Court therefore DENIES the motion for summary judgment of non-infringement.

II. The Motion for Summary Judgment of Invalidity

The defendants argue that if the '124 patent claims are not restricted to the specific compounds disclosed in the specification, the specification fails to satisfy the "written description" requirement of 35 U.S.C. § 112 ¶ 1, and the asserted claims are invalid.

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that those sources of guidance as to the meaning of the claims indicate that the claim language must be construed to refer to a selective inhibitor of PDE V.

Section 112 paragraph 1 provides, in pertinent part:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same . . . .

35 U.S.C. § 112 ¶ 1 (2006). That provision has remained largely unchanged since the Patent Act of 1793.[8]

The written description clause has been interpreted to require that the specification "describe the invention sufficiently to convey to a person of skill in the art that the patentee had possession of the claimed invention at the time of the application, i.e., that the patentee invented what is claimed." Ariad Pharms., Inc. v. Eli Lilly & Co., 598 F.3d 1336, 1345 (Fed. Cir. 2010) (en banc).[9] The level of detail required to satisfy the written description requirement "varies depending on the nature and scope of the claims and on the complexity and predictability of the relevant technology." Id. at 1351; see also Capon v. Eshhar, 418 F.3d 1349, 1357 (Fed. Cir.

[8] See Act of Feb. 21, 1793, 1 Stat. 318, 319 (the applicant "shall deliver a written description of his invention, and of the manner of using, or process of compounding the same, in such full, clear and exact terms, as to distinguish the same from all other things before known, and to enable any person skilled in the art or science . . . which it is most nearly connected, to make, compound and use the same").

[9] As the Federal Circuit explained in Ariad, 598 F.3d at 1351, the possession inquiry is an objective one that is viewed from the perspective of a person of ordinary skill in the art:

> The term "possession" . . . has never been very enlightening. It implies that as long as one can produce records documenting a written description of a claimed invention, one can show possession. But the hallmark of written description is disclosure. Thus, "possession as shown in the disclosure" is a more complete formulation. Yet whatever the specific articulation, the test requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art. Based on that inquiry, the specification must describe an invention understandable to that skilled artisan and show that the inventor actually invented the invention claimed.

2005) (what is required "varies with the nature and scope of the invention at issue, and with the scientific and technologic knowledge already in existence"). In the case of a claim to a genus, the Federal Circuit has held that "a sufficient description of the genus . . . requires the disclosure of either a representative number of species falling within the scope of the genus or structural features common to the members of the genus so that one of skill in the art can 'visualize or recognize' the members of the genus." Ariad, 598 F.3d at 1350.

Whether the written description requirement is satisfied is a question of fact. Scriptpro, LLC v. Innovation Assocs., Inc., 762 F.3d 1355, 1359 (Fed. Cir. 2014). The failure to satisfy the requirements of 35 U.S.C. § 112 ¶ 1 must be proved by clear and convincing evidence. AbbVie Deutschland GmbH & Co., KG v. Janssen Biotech, Inc., 759 F.3d 1285, 1297 (Fed. Cir. 2014).

The defendants argue that they are entitled to summary judgment on the written description issue. Summary judgment is appropriate when there are no genuine issues of material fact and when, drawing all factual inferences in favor of the nonmoving party, no "reasonable jury could return a verdict for the nonmoving party." Anderson v. Liberty Lobby, Inc., 477 U.S. 242, 248 (1986); accord Scriptpro, 762 F.3d at 1359. Even under the clear and convincing evidence standard, the defendants contend, a reasonable jury would be compelled to find that the specification of the '124 patent provides an inadequate written description of the invention set forth in the claims.

In particular, the defendants argue that UroPep's proposed construction of the term "inhibitor" encompasses a great number of compounds, including many that are not disclosed in the patent or in the prior art, and many that have not even been discovered. UroPep's "overreaching construction," according to the defendants, "far exceeds the disclosure of the '124 patent and if adopted, renders claims 1 and 3 of the '124 patent invalid." Eli Lilly & Co.'s and

Brookshire Brothers, Inc.'s Mot. for Partial Summ. J. that Claims 1 and 3 of U.S. Patent No. 8,791,124 Are Invalid for Failure to Meet the Written Description Requirement of 35 U.S.C. § 112 ¶ 1 and Mem. of Law in Support Thereof, at 10, Dkt. No. 120.

The Court concludes that there is at least a disputed issue of material fact as to whether the '124 patent specification satisfies the written description requirement. In the first place, the claims of the '124 patent are directed to the use of PDE V inhibitors to treat BPH, not to the discovery of PDE V inhibitors themselves. As UroPep explains, the "inventors did not purport to, and did not, contribute novel PDE V inhibitors" to the art. See Pl. UroPep's Combined Opp'n to Defs.' Mots. for Summ. J., at 22, Dkt. No. 129. Given the nature of the claims, the proper inquiry under the written description requirement is whether the disclosure in the specification shows that the inventors possessed the invention that administering an effective amount of a PDE5 inhibitor would treat BPH. Thus, given that at least some PDE V inhibitors were known and were disclosed in the '124 specification, the written description issue does not turn on whether the patentees were in possession of the entire genus of PDE V inhibitors.

In re Herschler, 591 F.2d 692 (C.C.P.A. 1979), presented a similar issue. In that case, the court found adequate written description support for broad claims for topically administering a steroidal agent by administering the steroidal agent together with dimethyl sulfoxide. Even though the specification disclosed only a single example of a steroidal agent, the court found that the disclosure was sufficient because the claim was drawn to the method of administering the steroidal agent, and numerous active steroidal agents were known to persons of skill in the art. 591 F.2d at 701. The court noted that "[w]ere this application drawn to novel 'steroidal agents,' a different question would be posed." Id.; see also Rochester, 358 F.3d at 928 (discussing Herschler).

To the same effect is In re Fuetterer, 319 F.2d 259 (C.C.P.A.) (Rich, J.), in which the application was directed to a combination of substances used to make rubber tire tread stock, including "an inorganic salt that is capable of holding a mixture of . . . carbohydrate and protein in colloidal suspension in water." Id. at 261. The Patent Office Board of Appeals rejected the representative claim on the ground that it was functional and because the specification included only four examples of such salts. Id. at 262. The court reversed the Board. In his opinion, Judge Rich explained that the "invention is the combination claimed and not the discovery that certain inorganic salts have colloid suspending properties." Id. at 265. He continued, in words applicable here by analogy,

> We see nothing in patent law which requires appellant to discover which of all those salts have such properties and which will function properly in his combination. If others in the future discover what inorganic salts additional to those enumerated do have such properties, it is clear appellant will have no control over them per se, and equally clear his claims should not be so restricted that they can be avoided merely by using some inorganic salt not named by appellant in his disclosure.

Id.

UroPep's evidence shows that PDE V inhibitors were not unknown as of the July 9, 1997, priority date of the '124 patent. To the contrary, there were hundreds of known PDE V inhibitors at that time. Accordingly, the written description requirement is satisfied if the specification shows that the inventors possessed the method of treating BPH by administering an inhibitor of PDE V.

Relying on language from Rochester and AbbVie, the defendants assert that the written description requirement applies "[r]egardless whether a compound is claimed per se or a method is claimed that entails the use of the compound[]." See Rochester, 358 F.3d at 926. That statement was made in a different context, however. The claims at issue in that case were

directed to methods "for selectively inhibiting PGHS-2 activity in a human host." 358 F.3d at 918. In that context, it made sense for the court to say that the written description requirement was the same whether the claims were directed to inhibitors of PGHS-2 activity or to methods of inhibiting PGSH-2 activity, as the essence of the invention was the same in both cases—the identification of compounds that would inhibit PGHS-2 activity.

In this case, by contrast, the invention is not a method for inhibiting PDE V, which would be analogous to the invention in the Rochester case. Instead, the invention is a method of treating BPH by using inhibitors of PDE V. Because the invention is not the identification of particular inhibitors, but the use of compounds having the inhibiting feature for a particular therapeutic purpose, the particular risk presented in Rochester—that the inventor is seeking claim coverage for a genus of compounds that perform a particular function, while only disclosing a small and unrepresentative subset of such compounds—is not directly presented here.[10]

These distinctions of the Rochester and AbbVie cases might not have much force if the specification of the '124 patent had disclosed very little information about PDE V inhibitors, or had provided no examples of such inhibitors. In that setting, it could be argued that, absent knowledge of the substances to be used in the claimed treatment, the inventors were not shown to be in possession of the invention.

[10] The same distinction applies to the AbbVie case on which the defendants rely. 759 F.3d 1285. The claims in that case were drawn to isolated antibodies that would neutralize the activity of human interleukin 12, and the patent purported to teach how to make such antibodies. The examples given in the patent, however, were limited to certain species of the claimed antibodies, even though the claims were not so limited, and the specification did not disclose structural features common to the members of the claimed genus of antibodies. 759 F.3d at 1299. Under these circumstances, the Federal Circuit upheld the jury's verdict that the written description requirement was not satisfied.

Indeed, the patent in Rochester did "not disclose any compounds that [could] be used in its claimed methods"; the court explained that "[w]ithout such disclosure, the claimed methods cannot be said to have been described." 358 F.3d at 927. The court distinguished the case before it from other cases in which the specification also failed to cite examples but was nevertheless held sufficient because persons of skill in the art "could recognize what was being claimed" based on the prevailing knowledge. Id. at 928 (discussing, e.g., Union Oil Co. v. Atlantic Richfield Co., 208 F.3d 989 (Fed. Cir. 2000), where "evidence was adduced . . . that artisans skilled in petroleum refining were aware of the properties of raw petroleum sources and knew how to mix streams of such sources to achieve a final product with desired characteristics."). In Rochester, the lack of examples and anything beyond a "vague functional description" meant that the patent was drawn to no more than "a mere wish or plan for obtaining the claimed chemical invention." Id. at 927.

In this case, however, the disclosures in the specification regarding PDE V inhibitors go beyond merely providing a functional description, or only a single example, of a PDE V inhibitor. As noted above, the '124 specification contains a description of the biochemistry underlying the invention. It discloses that the relaxation of smooth muscle cells in the prostate can result in a distinct improvement in the symptoms of BPH. It discloses the physiological mechanism by which information is transmitted that causes the relaxation of smooth muscle cells, explaining that hormones or neurotransmitters cause an increase in cAMP and cGMP in the smooth muscle cells, resulting in relaxation of those cells. It explains that because cAMP and cGMP are hydrolyzed by phosphodiesterases, inhibitors of PDEs reduce the digestion of cAMP and cGMP, "resulting in an increase in these molecules within the cell and thus in a relaxation of the smooth muscle cell." '124 patent, col. 1, ll. 36-47.

The specification teaches that three specific PDEs—PDE I, PDE IV, and PDE V—"are of particular importance in human prostatic muscles." Id., col. 2, ll. 6-8. The specification then concludes that a "well-aimed inhibition of these isoenzymes will result in relaxation of the prostatic muscles even when minute doses of a specific inhibitor are administered, with no appreciable effects in other organ strips, particularly vessels, being observed. Therefore, they have an excellent efficiency in the treatment of prostatic diseases." Id., col. 2, ll. 11-16. The specification lists 12 "preferred selective inhibitors" of PDE I, IV, and V: 10 compounds and two general names of compounds. The journal articles cited in the specification (and the sources cited in those journal articles) disclose other PDE V inhibitors. See C. David Nicholson & M. Shadid, Inhibitors of Cyclic Nucleotide Phosphodiesterase Isoenzymes–Their Potential Utility in the Therapy of Asthma, 7 PULM. PHARMACOL., no. 1, 1994, at 1-17; T. J. Torphy et al., Identification, Characterization and Functional Role of Phosphodiesterase Isoenzymes in Human Airway Smooth Muscle, 265 J. PHARMACOL. EXP. THER., no. 3, 1993, at 1213-23; W. J. Thompson, Cyclic Nucleotide Phosphodiesterases: Pharmacology, Biochemistry and Function, 51 PHARMACOL. THER., no. 1, 1991, at 13-33.

Beyond that, the specification describes in some detail pharmacological studies that were used to determine the potency of specific PDE inhibitors. '124 patent, col. 7, ll. 14-34. Those studies involved the use of samples of human prostatic tissue in a solution of a specific PDE inhibitor to measure the degree of muscle relaxation caused by particular test compounds. The results of those studies showed that "the inhibitors of PDE I, IV and V proved to have the strongest prostatic tissue relaxing effect." Id., col. 7, ll. 32-34.

The specification also states that "the proof of whether a compound is suitable for the purpose according to the invention" is furnished by known methods, citing references from 1989

and 1990. '124 patent, col. 7, ll. 35-39. The specification then describes an assay for determining if a substance is an inhibitor of a specific PDE and determining the potency of that inhibitor. Id., col. 7, line 35, through col. 8, line 16. UroPep points to record evidence that the information provided by that assay would be sufficient to show that the particular inhibitor under examination would have the necessary potency to be therapeutically effective against BPH. Bell Dep., at 111:2-6, 114:15-20 (Aug. 11, 2016), Dkt. No. 140-1. The information provided regarding PDE inhibitors in general, and PDE V inhibitors in particular, is considerably more detailed than the information disclosed regarding the genus of PGSH-2 inhibitors in Rochester and antibodies that could neutralize interleukin 12 in AbbVie.

To be sure, there is much that the '124 specification does not describe. For example, it does not separately discuss the characteristics of the three identified specific phosphodiesterases, PDE I, PDE IV, and PDE V. Other than the general statement that specific PDEs are distributed differently throughout the body, the specification provides no explanation of how or why one of those three PDEs should be targeted differently within prostate tissue. That is to say, despite the fact that the claims of the '124 patent are directed only to PDE V, the specification provides no suggestion as to why a person of ordinary skill would single out PDE V rather than the other two PDE inhibitors of interest, PDE I and PDE IV. See Defs. Eli Lilly & Co. and Brookshire Brothers, Inc.'s Consolidated Reply Br. in Support of their Mots. for Summ. J. of Noninfringement and for Invalidity for Failure to Meet the Written Description Requirement of 35 U.S.C. § 112, ¶6, at 15, Dkt. No. 139. The specification also provides no substantive results for the tests it discusses or the results of any testing demonstrating actual prophylaxis or treatment of BPH in animals or humans.

In response to the defendants' criticisms of the disclosure in the '124 specification, UroPep points out that in assessing the adequacy of a specification's disclosure for written description purposes, the Court must view the disclosure as would one of skill in the art. See Ariad, 598 F.3d at 1351 (Possession means possession as shown in the disclosure and "requires an objective inquiry into the four corners of the specification from the perspective of a person of ordinary skill in the art."); In re Alonso, 545 F.3d 1015, 1019 (Fed. Cir. 2008); Intel Corp. v. VIA Techs., Inc., 319 F.3d 1357, 1365-66 (Fed. Cir. 2003). Because "the patent specification is written for a person of skill in the art, and such a person comes to the patent with the knowledge of what has come before . . . it is unnecessary to spell out every detail of the invention in the specification; only enough must be included to convince a person of skill in the art that the inventor possessed the invention . . . ." LizardTech, Inc. v. Earth Res. Mapping, Inc., 424 F.3d 1336, 1345 (Fed. Cir. 2005).

UroPep points to evidence in the record that persons of skill in the art would have been aware of hundreds of PDE V inhibitors in addition to the exemplary compounds set forth in the '124 specification, see the evidence cited at pages 15-16, supra. UroPep also points to evidence that persons of skill in the art would have been aware of the structure of tadalafil, the compound used in the defendants' accused method, and the fact that tadalafil is a PDE V inhibitor, see Rotella Decl., at ¶ 64; Bell Decl., at ¶ 46; Rotella Dep., at 48:18-22.

It was not necessary for the patentees to include in the specification a catalog of all then-known PDE V inhibitors, UroPep argues, because persons of skill in the art were aware of the studies listing large number of such inhibitors. In light of the knowledge of persons in the field at the time, according to UroPep, the particular PDE V inhibitors that were described in detail in the specification constitute "a representative number of species falling within the scope of the

genus," AbbVie, 759 F.3d at 1299, even if the genus is viewed as all compounds capable of inhibiting the catalytic action of PDE V.

Whether the omissions from the specification, viewed in light of the facts known to persons of skill in the art as of the priority date of the '124 patent, render the specification insufficient to provide the necessary written description of the inventions of the '124 patent is a factual issue. The Court is persuaded that what is disclosed in the specification, when viewed in light of what a person of ordinary skill in the art would have known at the time, is sufficient to at least raise a question of fact sufficient to take the written description issue to a jury. The Court therefore DENIES the defendants' motion for partial summary judgment of invalidity based on 35 U.S.C. § 112 ¶ 1.

IT IS SO ORDERED.

SIGNED this 21st day of October, 2016.

William C. Bryson

WILLIAM C. BRYSON
UNITED STATES CIRCUIT JUDGE